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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 14

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
10662-86PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00483	27/04/2000	28/04/1999
International Patent Classification (IPC) or national classification and IPC C12N15/00		
Applicant UNIVERSITE DE MONTREAL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☒	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/11/2000	28.06.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Roscoe, R Telephone No. +49 89 2399 2554

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00483

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-15	as originally filed			

Claims, No.:

1-38	as received on	30/05/2001	with letter of	30/05/2001

Drawings, sheets:

1/1	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed.

   ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

   Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
   see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5, 32
	No:	Claims	1-4, 6-31, 33-37
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-38
Industrial applicability (IA)	Yes:	Claims	25-27
	No:	Claims	1-24, 28-38

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

I. Basis

The documents mentioned in the present written opinion / International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

II. Priority

Priority could not be acknowledged for those claims which make reference to activation of oocytes by (i) natural means, (ii) physical means, (iii) by specific listed physical means, or to claims referring to specific cell-cycle stages (G0, G1, S...). The use of this terminology cannot be detected in the priority document, neither is it obviously derivable therefrom. The fact that it may be possible to infer this matter from the priority document is not sufficient to establish priority.

Only the following claims are thus entitled to priority from 28.04.99:

Claims 1, 3, 5, 7-9, 13, 15-18, 28, 31, 33-35, 37 and 38

V. Reasoned statement on Novelty, Inventive Step and Industrial Applicability

- Novelty (Art.33(2) PCT)

D1 discloses enucleation technique where oocytes are activated using ethanol. This is followed by microsurgical removal of the telophase-stage chromatin in a small volume of cytoplasm adjacent to the second polar body. Following enucleation, a single blastomere derived from an in vitro produced morulla was injected into the perivitelline space of the enucleated oocyte. Fusion of the membranes was performed by electrical pulsing. The reconstructed oocytes obtained by the new technique produced developmentally competent reconstructed oocytes. Technique suggested to be useful for research and practice of mammalian cloning. D1 relates specifically to cloning of animals using early embryonic blastomeres. Such cells can be considered as having the status of both germinal or somatic. Unspecified periods of culture can obviously not establish a difference between this prior art and the present application since

unless specific times are defined which clearly differentiate from the prior art, the unspecified periods have to be considered as an unclear and thus irrelevant technical feature.

D1 anticipates claims 10-13, 15-18, 20, 21, 25, 28-31, 33-37.

D2 discloses enucleation technique which differs from the D1 technique essentially in that sequential calcium ionophore and cycloheximide treatment are used to activate oocytes. Further, it is specified explicitly that both recipient ooplast and donor blastomeres are probably effectively in S-phase. Suggests that use method to produce large numbers of identical progeny. D2 does not only relate to metaphase II enucleation. D2 compares enucleation efficiency before and after oocyte activation. Already in the abstract it is stated that 100% of chromatin material was found adjacent to the second polar body after the activation. This is clearly referring to oocytes that have proceeded beyond metaphase II to the telophase II at which the extrusion of the second polar body is evident. Applicants attention is also drawn to the first two paragraphs of the results section.

D2 anticipates claims 10-12, 15-18, 20, 21, 25, 28-30, 33-37.

D3 discloses a different enucleation technique. However anticipates claims 25-27, since embryos / animals / offspring are not distinguishable whether produced by method involving enucleation at 1st or 2nd polar body.

D4 discloses production of transgenic sheep. Anticipates claims 25-27.

D6 is only relevant to claims other than 1, 3, 5, 7-9, 13, 15-18, 28, 31, 33-35, 37 and 38 (see section on priority). D6 discloses electrofusion of transgenic somatic goat cells with oocytes which have been enucleated at Tel-II stage after activation by (i) calcium, (ii) ethanol. Animals were derived from protocol (i), but none of embryos survived to day 40 from protocol (ii). Argumentation relating to in vivo matured oocytes is not followed (a distinguishing feature based on this is not in the claims anyway). Further, the data relating to calcium-activated oocytes cannot be ignored - this provides a working protocol with surviving embryos. Animals

clearly could be obtained derived from the calcium-activated cells.

D6 anticipates claims 10-12, 19-24, 29, 30, 36.

- **Inventive Step (Art.33(3) PCT)**

Only claims 5 and 32 appear to be novel. Claims 5 and 32 are novel due to the physical means used for oocyte activation. However, the oocyte activation protocols used by applicant and claimed were all known to the skilled person - physical methods just being a trivial selection from a number of known possibilities.

Hence, at present, no inventive subject-matter can be detected in the present application.

Applicants argumentation could not be followed.

- **Industrial Applicability (Art.33(4) PCT)**

For the assessment of the present claims 1-24 and 28-38 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 1-24 and 28-38 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

VIII. **Certain observations**

Claims 25-27 include the manipulation of human embryos in their scope (since these claims have been amended in a manner which uncouples them from claims refering to non-human cells. This subject-matter is considered by the present IPEA to be contrary to morality and hence not allowable. Applicant is reminded to be very careful when dealing with such matters as inclusion of matter relating to human embryos can lead to major consequences should such matter proceed to grant in a subsequent regional procedure.

- **Clarity (Art.6 PCT)**

Claims 25-27 are unallowable product-by-process claims. The resulting embryo does not retain any features imparted by the particular method by which it was produced. Hence, these claims need to be deleted.